# Bandolier 106

## Independent evidence-based health care

Questions *Bandolier* receives from readers are many and varied. For many there is no simple and quick answer, and for others there is information available on the *Bandolier* Internet site, or quickly available in the literature. This month *Bandolier* responds to readers' questions that needed a bit of digging.

Following an earlier article in the NICE report on anti-TNF agents for rheumatoid arthritis (*Bandolier* 99), a junior doctor asked about evidence of efficacy in ankylosing spondylitis and other conditions. For ankylosing spondylitis the evidence seems to be mounting, with three relevant randomised trials and a review of all studies of any architecture to date. It is even possible to generate an NNT (of 2) for useful outcomes over about 12 to 16 weeks. Obviously more information is needed, but it looks promising.

*Bandolier* 103 reported on nursing levels and complications in ITU, prompting requests for more of the same. While there's not a huge literature, it was interesting to see a large study on nurse staffing levels and patient and nurse outcomes in Pennsylvania.

There are the common questions, often asked, like the level of use of retail analgesics in the community, and about the optimum INR level. And the uncommon, about links between an obscure preservative in cosmetics and household products and contact dermatitis. We found information on all three.

## Needlestick injuries

A new feature on the *Bandolier* Internet site is a section devoted to the evidence around needlestick injuries. *Bandolier* has scoured the literature, and has begun to summarise it. There is quite a lot known, and occasionally it has been pulled together. The bottom line so far is that it is a bigger problem than we realised, but with varying consequences and costs. Over the next few months the site will continue to grow.

### In this issue



## Anti-TNF for ankylosing spondylitis

A *Bandolier* reader asked whether it was true that anti-TNF treatments used for rheumatoid arthritis also worked for ankylosing spondylitis, and whether there was any evidence? "True" is one of those deeply philosophical words to shy away from on grey November mornings, but evidence there is.

A thorough, if not systematic, review [1] examines the rationale for using anti-TNF therapy. It also looks at clinical studies published to date. In open-label and randomised trials 268 patients with ankylosing spondylitis for five to 17 years (trial average) have received therapy for 10 weeks to a year. Most information is with infliximab, but there is also some with etanercept. All the studies, some of which included other patients with spondyloarthritis, show big reductions in one of the main outcome scores.

The Bath ankylosing spondylitis disease activity index (BASDAI) measures disease activity on the basis of six questions relating to fatigue, spinal pain, peripheral arthritis, enthesitis (inflammation at the points where tendons/ligaments/joint capsule enter the bone), and morning stiffness. The review reports that in eight studies with infliximab (two randomised) the median reduction in the BASDAI score was between 55% and 93% at longest duration. The two studies with etanercept (one randomised) reported 51% and 79% median reductions.

Given these apparently very good results a look at the randomised trials seemed worthwhile.

## Infliximab in ankylosing spondylitis [2]

Patients in the study were those with active ankylosing spondylitis according to defined (New York) criteria, a BASDAI score of 4 or more and spinal pain of 4 or more on a 10 cm scale (approximating at least moderate pain). Exclusions were sensible. DMARDs and steroids were withdrawn four weeks before randomisation, but NSAIDs were continued, and dose reductions but not increases allowed. After randomisation pharmacists prepared unlabelled drugs, but investigators and patients were unaware of allocation.

Intravenous infliximab was infused at 5 mg/kg at the start of the study and at two and six weeks. A battery of outcomes was used for efficacy, administered at baseline, and at two, six and 12 weeks. The primary outcome was improvement in disease activity measured by BASDAI change of 50% between baseline and the 12-week observation.

### Results

The 69 patients had a mean age of about 40 years with mean disease duration of 15 years, and mean pain score at baseline was 7 on a 10 cm scale (approximating to severe pain). The primary outcome was achieved by 17/34 patients on infliximab and 2/35 on placebo, and the difference between placebo and infliximab was apparent by the second week. The number needed to treat for one patient to have the outcome at 12 weeks who would not have had it if treated with placebo was 2.3 (95% confidence interval 1.6 to 3.9). NSAIDs were reduced to less than 50% of baseline dose in 18/34 patients on infliximab and 6/35 on placebo. NSAIDs were stopped completely in 13/34 patients on infliximab and 4/35 on placebo. Other outcomes, like ESR, CRP, pain scores and other indices of disease, all showed large and significant improvements.

Three patients on infliximab had serious events and were withdrawn due to emergent tuberculosis, fever, and transient leucopenia. All three had significantly improved during infliximab treatment.

## Etanercept in ankylosing spondylitis [3]

Patients in the study were those with active ankylosing spondylitis according to defined (New York) criteria, with morning stiffness of at least 45 minutes and at least moderate disease activity. Prescribed drugs, including corticosteroids and DMARDs were continued. Exclusions were sensible.

Randomisation was to twice-weekly subcutaneous injections of placebo or 25 mg etanercept for four months, with monthly assessments. A battery of efficacy assessments was used, but the primary outcome was a composite treatment response of 20% or greater improvement in at least three of five measures of disease activity (morning stiffness, nocturnal pain, Bath functional index, patient global assessment of disease activity and score for joint swelling). The trial was described as double-blind, with no details given.

### Results

The average age was 39 years, with mean disease duration of 12 years, and with a minority of patients taking steroids or DMARDs. Treatment response was seen in 16/20 patients treated with etanercept and 6/20 treated with placebo. The number needed to treat for one patient to have the outcome at 16 weeks who would not have had it if treated with placebo was 2.0 (95% confidence interval 1.3 to 4.3). Baseline treatments were not altered in the trial, but in an open label extension, about two-thirds of patients discontinued or decreased doses of corticosteroids, DMARDs and NSAIDs. Other outcomes, like ESR, CRP, pain scores and other indices of disease all showed large and significant improvements. Patients given placebo in the randomised trial went on to do well in an open label extension.

Three patients withdrew, one on etanercept for personal reasons and two on placebo for lack of efficacy. There were no withdrawals because of adverse events.

## Infliximab in active spondylarthropathy [4]

Patients in this study had to fulfil the European spondylarthropathy group criteria, and had to have active disease at enrolment, defined as at least one swollen joint or current episode of active tendinitis or dactylitis and/or inflammatory spinal pain. Prescribed NSAIDs and corticosteroids could be maintained.

Intravenous infliximab was infused at 5 mg/kg at the start of the study and at two and six weeks. A battery of outcomes were used for efficacy, administered at baseline, and at two, six and 12 weeks. Primary outcomes were patient and physician global assessment of disease.

### Results

The average age of patients was in the late 40s, and 19 of the 40 patients had ankylosing spondylitis. Others had psoriatic arthritis or undifferentiated spondylarthropathy. Most patients were using NSAIDs. Patient global assessment of

**Table 1: Individual trial and combined NNTs**

| Patients | Treatment | Number improved/total | | Relative benefit (95% CI) | NNT (95% CI) |
|---|---|---|---|---|---|
| | | Treatment | Placebo | | |
| Ankylosing spondylitis | Infliximab | 17/34 | 2/35 | 8.8 (2.2 to 35) | 2.3 (1.6 to 3.9) |
| Ankylosing spondylitis | Etanercept | 16/20 | 6/20 | 2.7 (1.3 to 5.4) | 2.0 (1.3 to 4.3) |
| Active spondylarthropathy | Infliximab | 17/20 | 3/20 | 5.7 (2.0 to 16) | 1.4 (1.1 to 2.1) |
| Combined data | | 50/74 | 11/75 | 4.6 (2.6 to 8.0) | 1.9 (1.5 to 2.5) |

disease measured on a 100 mm VAS was significantly reduced by week 2 of the 12 week period, and improved further subsequently (Figure 1). Placebo scores were unchanged.

Major improvement in global assessment was experienced by 17/20 patients treated with infliximab, compared with 3/20 experiencing some improvement with placebo. The number needed to treat for one patient to have the outcome at 12 weeks who would not have had it if treated with placebo was 1.4 (95% confidence interval 1.1 to 2.1).

There were two serious adverse effects with infliximab, resulting in withdrawal. One patient developed active tuberculosis, and one a septic knee after needle arthroscopy. Both had improved before withdrawal.

**Figure 1: Patient global assessment of disease over 12 weeks**

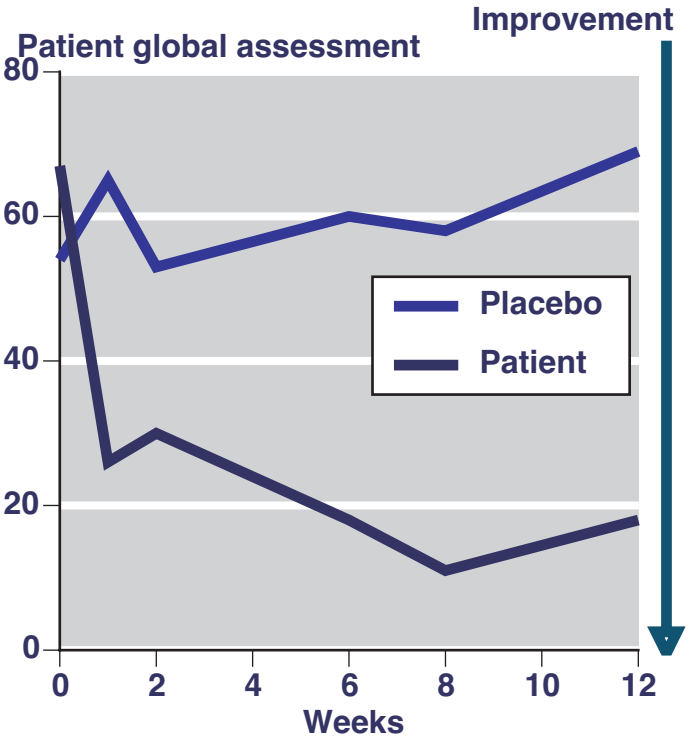
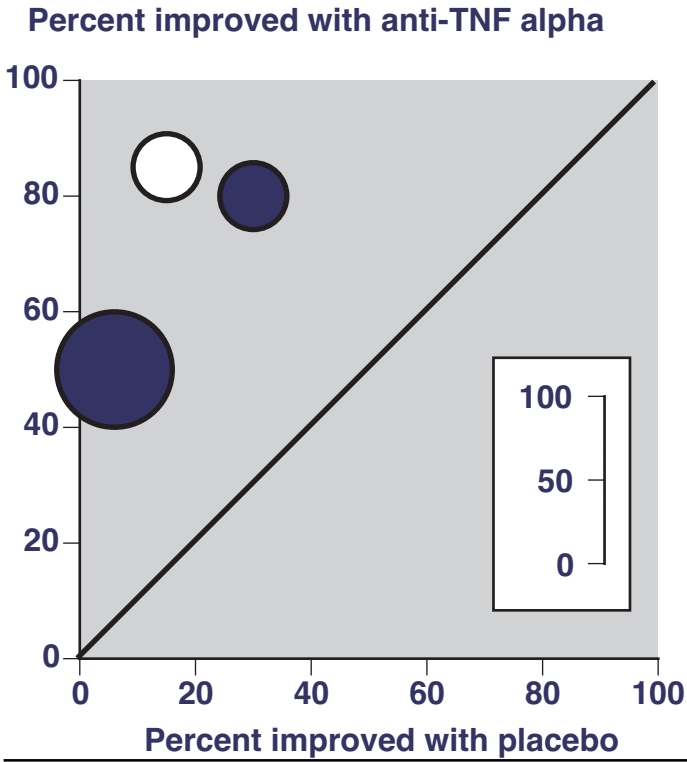



**Figure 2: L'Abbé plot of trials of TNF-antagonists in spondylarthropathies. Filled circles ankylosing spondylitis patients only**




## Comment

These results look good. If we combine them as three studies of anti-TNF agents in active spondylarthropathies, mainly represented by ankylosing spondylitis, then the results can be seen in Figure 2 and Table 1. Despite different outcomes being used, 50/74 patients improved with anti-TNF agents. Five more improved but were withdrawn because of adverse events. That is a high response rate for high degrees of improvement in a condition that is difficult to treat, and in patients with active disease who have often had it for many years.

There was a downside, mainly associated with the risk of infection with TNF suppression. There were two cases of active tuberculosis, despite baseline screening.

At the end of 2002, no licence for the use of these agents in ankylosing spondylitis had been granted, and probably not even been sought. If the results were confirmed and drugs licensed for this indication, it could have major implications for prescribing costs. It seems to be good news for patients.

There are, of course, the linked issues of how good were the trials, and how much information we have. These are really important when we look at what amounts to preliminary information.

First, there is a good biological background to using anti-TNF agents for ankylosing spondylitis [1]. This is not an idea from the blue. The three trials were randomised, apparently double-blind, and reported withdrawals, so they would score a minimum of 3 out of 5 on a trial reporting scale. This makes them unlikely to suffer bias. The total number, at about 150 patients, is a little small for us to be completely certain of the effect of treatment, despite an apparently excellent response. So early, but encouraging, days.

References:


1 J Braun et al. Anti-tumour necrosis factor alpha therapy for ankylosing spondylitis: international experience. Annals of Rheumatic Disease 2002 61 (Suppl III): iii51-iii60.

2 J Braun et al. Treatment of active ankylosing spondylitis with infliximab: a randomised controlled multicentre trial. Lancet 2002 359: 1187-1193.

3 JD Gorman et al. Treatment of ankylosing spondylitis by inhibition of tumour necrosis factor alpha. New England Journal of Medicine 2002 346: 1349-1356.

4 F Van den Bosch et al. Randomized double-blind comparison of chimeric monoclonal antibody to tumor necrosis factor alpha (infliximab) versus placebo in active spondylarthropathy. Arthritis & Rheumatism 2002 46: 755-765.

# Optimum INR level?

Large, comprehensive linkage studies can provide useful information about various aspects of healthcare. Many come from Sweden, and the latest [1] provides much information about the INR levels and mortality.

## Study

The computerised records of 42,000 patients attending 46 anticoagulation clinics in the years 1990-1997 formed the basis of the study. Anticoagulation was being provided mainly for atrial fibrillation (58%), venous thrombosis and pulmonary embolism (25%), stroke and transient ischaemic attacks (22%), and valve prostheses (18%), or more than one of these indications.

Patient deaths were identified from a registry of causes of death, that included 99% of all deaths in Sweden. Contributing to this analysis were 3,553 deaths.

There were 1.25 million INR measurements. Each patient was followed from the time of an INR measurement to either the next INR, death, or for seven weeks. After this data were censored until a new INR measurement was performed.

**Figure 1: All cause mortality versus INR after 1.25 million INR measurements in 42,000 patients**

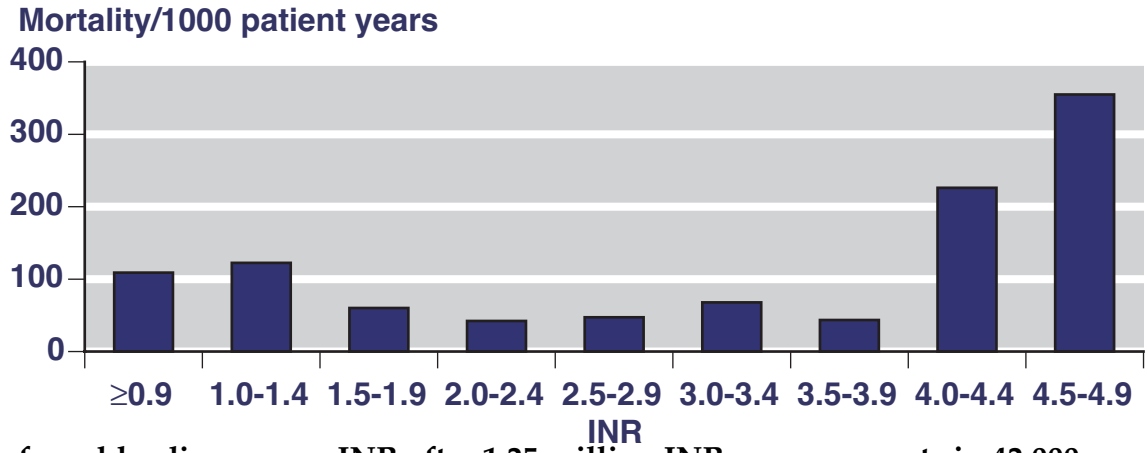
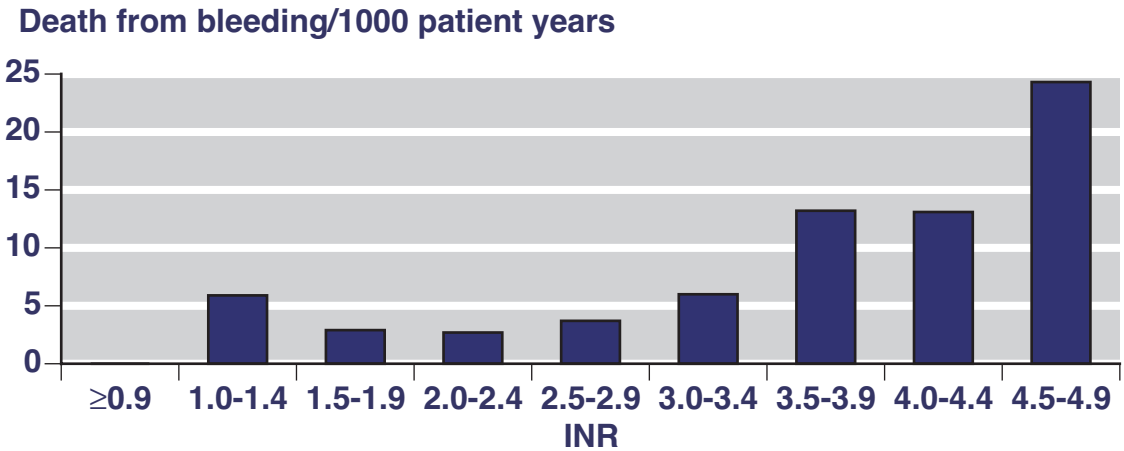



**Figure 2: Death from bleeding versus INR after 1.25 million INR measurements in 42,000 patients**




## Results

The average age of patients at the start of anticoagulation treatment was 71 years. The outcomes were mortality per 1,000 patient years, and death from bleeding per 1,000 patient years. Ascertainment for the latter as a cause of death was not complete because the fact of bleeding could not be confirmed in all patients.

All cause mortality was strongly related to the INR value. The lowest death rates were with INR values of 2.0 to 2.9 (Figure 1). Mortality was higher at INR values below 2.0. At INR values above 5.0, mortality was about 800 per 1,000 patient years.

Death caused by bleeding was also strongly related to INR. At INR values above 3.0 the rate increased rapidly (Figure 2).

## Comment

The authors concluded that mortality was lowest at INR values between 2.0 and 2.3. Mortality was not just from cerebral haemorrhage or bleeding, and other factors contributed more to all cause mortality. The window for optimal anticoagulation therapy was very narrow.

References:
1 A Odén, M Fahlén. Oral anticoagulation and risk of death: a medical record linkage study. BMJ 2002 325: 1073-1075.

# Methyldibromo glutaronitrile

*Bandolier* rarely visits the world of consumer products, but was prompted by a reader asking whether there was any known association between methyldibromo glutaronitrile and skin rash and itching. The answer is that there is, and the problem seems to be increasing.

Methyldibromo glutaronitrile is a preservative used in many cosmetics, shampoos, creams, and even some forms of toilet paper. It was introduced into Europe in the mid-1980s and in the early '90s into the USA. It comes by many other names, including the trade names Euxyl K 400, Tektamer 38, Merquat 2200, as well as other chemical names. The introduction of methyldibromo glutaronitrile was to replace preservatives known to be associated with a relatively high incidence of contact dermatitis in the range of 2-3%.

## Reports of contact dermatitis

The literature is rather well-endowed with case reports of contact dermatitis involving methyldibromo glutaronitrile, as well as several case series. These studies have been conducted in patients referred to dermatology clinics with skin or other complaints. Testing involves reasonably standard tests of patches of chemicals at one or more concentrations, and skin reactions judged to be irritant or allergic based on appearance and time course. Irritant reactions were those that tended to fade over 48-96 hours, and allergic reactions remained stable or increased in intensity.

Some of the reports are not immediately available, but a summary of the larger studies is in Table 1. In the early 1990s, methyldibromo glutaronitrile was associated with contact dermatitis in about 1% of patients, but this appears to have increased in Europe and the USA.

## A definite increase

Two longitudinal studies support the increase of sensitivity to methyldibromo glutaronitrile. Most important is an on-going study in 16 centres in 11 European countries examining the seven most commonly used preservatives [1] tested in patients with contact dermatitis. Levels of sensitivity for six of the preservatives remained constant over the period 1991-2000. Two ran at sensitivity levels of about 2% and the others at 1% or below. For methyldibromo glutaronitrile there was a sustained increase from under 1% at the start of this period to over 3.5% by the end (Figure 1). Another longitudinal survey in a London dermatology institute recorded large increases in sensitivity to methyldibromo glutaronitrile in the late 1990s [2].

**Table 1: Positive tests for methyldibromo glutaronitrile**

| Country | Period of testing | Number of subjects | Percent positive |
|---|---|---|---|
| USA | 1996-1997 | 163 | 4.9-7.9 |
| USA | 1994-1996 | 3,074 | 2.0 |
| Holland | 1994 | 2,943 | 4.0 |
| Holland | 1994 | 528 | 2.8 |
| Germany | 1990-1994 | 11,422 | 2.3 |
| Italy | 1991-1994 | 3,455 | 2.8 |
| Italy | 1991 | 2,057 | 1.2 |

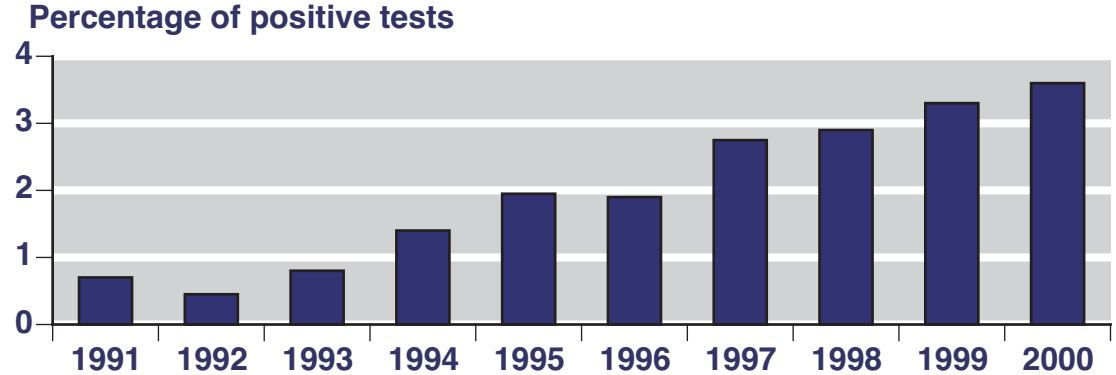
## Comment

A survey of a random selection of skin creams in Denmark in about 1999 showed only about 1 in 20 containing methyldibromo glutaronitrile [3]. A brief survey of ***Bandolier***'s local chemist shop seems to have many more products containing methyldibromo glutaronitrile. Skin creams, shampoos, shower gels, tanning creams, cucumber eye lotions, and protection creams are cosmetic products containing methyldibromo glutaronitrile. But it can also be found in industrial cleansers and a range of different materials.

Labelling should tell you whether or not it is present, but a survey [3] showed that while declared preservatives were within their permissible limits, some preservatives can be present, but not declared. So far this seems not to be the case with methyldibromo glutaronitrile.

References:
1 JD Wilkinson et al. Monitoring levels of preservative sensitivity in Europe. A 10-year overview (1991-2000). Contact Dermatitis 2002 46: 207-210.
2 JP McFadden et al. Increased rate of patch test reactivity to methyldibromo glutaronitrile. Contact Dermatitis 2000 42: 54-55.
3 SC Rastogi. Analytical control of preservative labelling on skin creams. Contact Dermatitis 2000 43: 339-343.

**Figure 1: Percentage of tests positive for methyldibromo glutaronitrile sensitivity in 16 centres in European countries in patients with contact dermatitis**



# Nurse staffing, mortality and burnout

An Audit Commission report in 2001 [1] could come to no conclusion whether nurse staffing levels on wards had any influence on clinical risk. Part of the reason was the paucity of data from UK hospital trusts that allowed that question to be addressed. An impressive large study from the USA [2] concludes that higher patient:nurse ratios leads to increased patient mortality, higher levels of nurse burnout, and nurse job dissatisfaction.

## Study

The study was conducted in Pennsylvania, and ultimately looked at staffing levels across 168 of 210 acute care hospitals with discharge data for surgical patients in targeted diagnosis-related groups of general surgery, orthopaedic surgery and vascular surgery. Hospital characteristics controlled for were size (≤100, 101-250 and ≥250 hospital beds), teaching status (none, minor or major teaching load), and high technology (open-heart surgery, or transplantation were measures of high technology).

Surveys were mailed to a 50% random sample of registered nurses in Pennsylvania, with a 52% response rate, and with 10,200 working in hospitals. There had to be at least 10 registered nurses returning a questionnaire from a hospital. Half the hospitals had more than 50 nurse respondents. The nurse staffing measure was taken from nurses who reported having responsibility for at least one but fewer than 20 patients on their last shift, regardless of time or specialty.

Discharge reports were obtained for 232,000 patients between the ages of 20 and 85 years over 18 months in 1998 and 1999. Outcomes used were 30-day mortality, and deaths within 30 days of admission among patients who experienced complications (pneumonia, hypotension, shock, for example).

## Results

The ratio of patients to nurses varied from 4:1 to 8:1, and the percentage of hospitals, nurses and patients in each category is shown in Figure 1. Almost 19 in 20 nurses were women, 4 in 10 had a nursing degree, and they had an average experience of 14 years in nursing.

**Table 1: Modelled effect of nurse staffing on patients**

| Patient:nurse ratio | Additional deaths per 1,000 patients | |
|---|---|---|
| | All patients | With complications |
| 6:1 rather than 4:1 | 2.3 | 8.7 |
| 8:1 rather than 6:1 | 2.6 | 9.5 |
| 8:1 rather than 4:1 | 5.0 | 18.2 |

Half the patients had undergone orthopaedic surgery, and nearly 40% digestive tract and hepatobiliary surgery. Some 54,000 (23%) experienced a major complication not present on admission, and 4,535 (2.0%) died within 30 days. In patients with complications 8.4% died.

Higher patient:nurse ratios were significantly associated with emotional exhaustion and greater job dissatisfaction. Increasing the ratio of patient to nurse by one increased burnout and job dissatisfaction by 23% and 15% respectively. An increase from 4:1 to 8:1 more than doubled job dissatisfaction. One in 10 nurses satisfied with their jobs intended to leave within 12 months. For dissatisfied nurses, this was closer to 1 in 2.

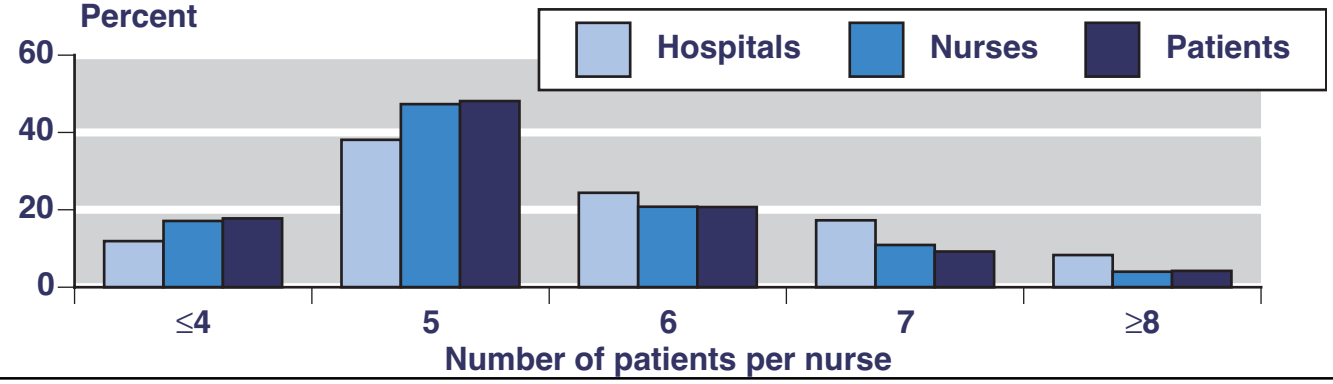
Higher patient:nurse ratios were significantly associated with patient mortality. Increasing the ratio of patient to nurse by one increased patient mortality by an average of 7%. Increases in nurse staffing from 4:1 to 6:1 or 8:1 would increase patient mortality by 14% and 31% respectively.

For Pennsylvania, the impact of nurse staffing on additional deaths for all patients and those with complications is shown in Table 1. With an average patient:nurse ratio of 4:1 to 8:1 there were 4,500 deaths. The implication of an overall patient nurse ratio of 4:1 would be 500 fewer deaths, and with a ratio of 8:1 there would be 500 more deaths over 18 months.

## Comment

The background to this paper is that in 2003 California will mandate that the patient:nurse ratio in its hospitals will not exceed 6:1, falling to no more than 5:1 when fully implemented. Someone, somewhere, is taking these issues seriously. Extrapolation of the Pennsylvania experience to California would mean 2,000 fewer deaths over 18 months.

**Figure 1: Distribution of patients per nurse in Pennsylvania**



Are we surprised that poor staffing levels lead to burnout, dissatisfaction, and a desire to leave the job? Perhaps not, but job satisfaction and burnout were specifically measured in this study. There is a standardised tool, the Maslach Burnout Inventory, and even a Burnout Inventory Manual. Someone, somewhere, is taking these issues seriously.

The interesting discussion in this paper refers to the high cost of staff replacement in the USA, and speculates that increasing staffing levels could not only save patient lives and decrease nurse turnover, but reduce hospital costs. Again, someone, somewhere, is taking this issue seriously.

A literature is beginning to appear from the USA, where they do take these issues seriously. ***Bandolier*** 103 looked at another US study showing that lower nurse staffing in the ITU resulted in more patient complications. In California they are saying that staffing levels and safety are linked, and that below a certain level safety is compromised and will not be tolerated. The implications of that train of thought are far-reaching indeed.

References:
1 Audit Commission. Acute hospital portfolio: review of national finding: ward staffing. 2001: 3.
2 LH Aiken et al. Hospital nurse staffing and patient mortality, nurse burnout, and job dissatisfaction. JAMA 2002 288: 1987-1993.

# OTC ANALGESICS – WHAT DO PEOPLE USE?

A number of issues come together to focus on what analgesics people use for common conditions, like headache, colds, aches and pains or period pains. One is safety, with paracetamol poisoning being a major driver in restricting pack size since 1998 in the UK. Another is increased concentration on the safety of aspirin and ibuprofen. A third would be the recognition that the vast majority of people use retail analgesics sensibly, and derive much benefit.

Almost any discussion of any of these topics raises the question of how many people use retail analgesics, and what sort, and how much. Satisfactory answers are few.

## How many people use retail analgesics?

***Bandolier*** 52 reported on a random sample of the Swedish population aged 16 years and older, who were asked specific questions relating to analgesic use [1]. The participation rate was 79%, and information was available from just under 12,000 people.

Overall about 20% of men and 30% of women used non-prescription analgesics. Use of non-prescription analgesics was similar in all age groups. There were some fairly obvious relationships. For instance, headache and musculoskeletal pain were associated with increased use of analgesics, as were high levels of physical work stress, poor physical fitness and perceived poor health. In the previous 12 months, 13% of men and 20% of women had visited alternative therapists.

## What analgesics are being used?

Annual sales of paracetamol, aspirin and ibuprofen, both by weight, pack, and pack size have been reported from a source (IMS Health) with census data on all wholesale sales to pharmacies and other retail outlets in the UK and Northern Ireland [2].

The total annual weight sold (in tonnes) is shown in Table 1 for 1998, 1999 and 2000. Of course, that's not quite the same as tablets, and the equivalent in 500 mg paracetamol, 300 mg aspirin and 200 mg ibuprofen tablets is shown in Figure 1. The information for aspirin is amended for the approximately 40% sold as 75 mg tablets (that's about 80 million 75 mg tablets in 2000).

**Table 1: Tonnes of retail analgesics sold each year in UK & NI**

| Year | Paracetamol | Aspirin | Ibuprofen |
|---|---|---|---|
| 1998 | 409 | 66 | 26 |
| 1999 | 199 | 22 | 30 |
| 2000 | 166 | 15 | 46 |

That works out to a reduction in analgesic use. Paracetamol use reduced significantly. Taking the UK adult population (over 12, say) to be about 51 million, on average each adult used 21 tablets in 1998, and 12 tablets each year in 1999 and 2000. The balance changed from a preponderance of paracetamol in 1998 to a rough parity between paracetamol 500 mg and ibuprofen 200 mg tablets in 2000. If about one adult in four uses retail analgesics, the total number of analgesic tablets for those who used them would be about 50 per year.

**Figure 1: Standardised retail tablet sales in UK & NI**

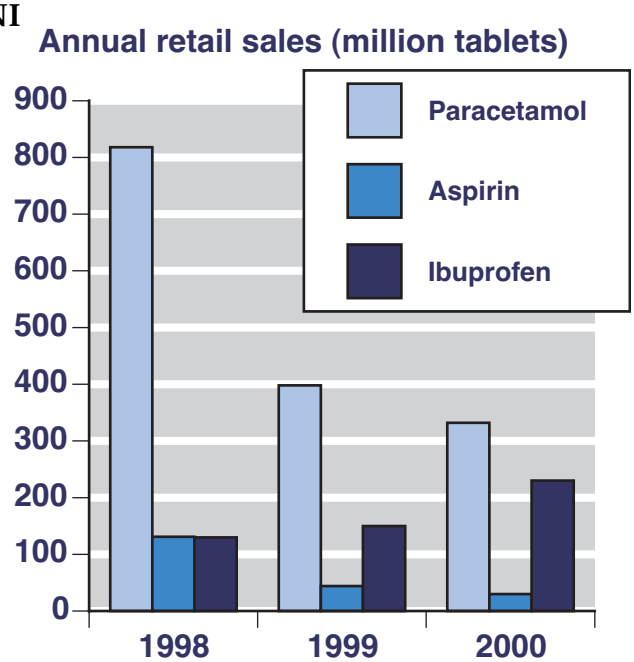


**Table 2: Summary of studies on paracetamol use and overdose after legislative change in UK & NI**

| Reference | Population | Measures | Outcomes |
|---|---|---|---|
| Prince et al. Lancet 2000 355: 2047-2048 | Newcastle and UK | Referrals to liver unit and UK transplant lists before and after September 1998, to December 1999 | Fall in referrals because of paracetamol overdose from 2.5 to 1 per month, and in UK Transplant Authority from 3.5 to 2 per month |
| Turvil et al. Lancet 2000 355: 2048-2049. | London | Incidence of paracetamol overdoses from Sept 1995 to August 1999 | 21% reduction in all paracetamol overdoses and 64% reduction in severe overdoses |
| Robinson et al. BMJ 2000 321: 926-927. | Belfast | Incidence of paracetamol overdose January-June 1998 and 1999 | No change in numbers of overdoses, admissions or severe liver failure, but reduced quantity taken and average serum paracetamol lower at 4 hours |
| Hawton et al. BMJ 2001 322: 1-7. | Five UK liver units and seven general hospitals, and England & Wales | Mortality, admissions, transplants, 24 months before and 12 months after change in legislation | Reduced number of deaths from paracetamol (21%), reduced admissions to transplant units, patients listed for transplant and transplantations due to paracetamol overdose, reduced number of overdoses due to paracetamol |

## Paracetamol overdoses affected?

Table 2 shows the immediate effects of restricting paracetamol pack size. Most show reduction in some aspect of paracetamol poisoning, though little effect was seen in Belfast. The largest and most through study showed a reduction by 21% in deaths from paracetamol overdose when taken alone compared with the average of the previous two years, down from about 190 to 150 cases a year for paracetamol alone [3]. It also showed reduced presentations, and admissions to transplant units and liver transplants.

## Comment

Discovering how consumers use retail analgesics is hardly easy, especially when markets are perturbed by legislation. The pack size restrictions introduced in September 1998 had effects before and after that date. Manufacturers had a year to change their manufacturing and distribution practices. Consumers may have bought supplies in advance of the legislation. Travel changes purchasing patterns, and visitors to the USA often return with large pots of paracetamol or ibuprofen, because it is available in large amounts at much lower cost.

What we can say is that consumer usage of paracetamol has dropped substantially, by more than half since 1998. Overdose statistics seem to reflect that change, but are available only from the first year after the change. Several more years will be needed to see the full effects.

Ibuprofen use has doubled. While ibuprofen overdose is not so much of a problem, the insidious nature of NSAID adverse events may mean that some of the more enthusiastic users could be putting themselves at risk, particularly from gastrointestinal problems.

Quantifying that risk is difficult. It is a tricky area, the literature is confused, and practice changes (like getting paracetamol on prescription because it is now expensive). ***Bandolier*** will revisit as more information comes our way.

References:
1 KIM Antonov, DGL Isacson. Prescription and nonprescription analgesic use in Sweden. Annals of Pharmacotherapy 1998 32: 485-94.
2 CL Sheen et al. Paracetamol pack size restriction: the impact on paracetamol poisoning and the over-the-counter supply of paracetamol, aspirin and ibuprofen. Pharmacoepidemiology and Drug Safety 2002 11: 329-331.
3 K Hawton et al. Effect of legislation restricting pack sizes of paracetamol and salicylate on self poisoning in the UK: before and after study. BMJ 2001 322: 1-7.

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ISSN 1353-9906